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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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CARELLA, BYRNE, BAIN, GILFILLAN, CECCHI,
STEWART & OLSTEIN
6 Becker Farm Road
Roseland, NJ 07068

EXAMINER	
SHAHNAN SHAH, KHATOL S	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,350	HULTGREN ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-65* is/are pending in the application.

4a) Of the above claim(s) *20-24,33-52,55-58,60 and 62,63 and 65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,25-32,53,54,61 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-65* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicants' election with traverse of November 26, 2003, is acknowledged. Applicants elected group I, claims 1-19, 25-32, 37-48, 53-54, 59-60 and 62-65 which are drawn to an isolated protein construct. Applicants have elected the protein construct of claim 1 as species. Applicants further elected sub- species the antibody vitaxin (of claim 64) and the anticancer agent (of claim 61). The traversal is on the ground(s) that searching for groups IV will not put additional burden upon the office when searching for elected group I, has been noted. This is not found persuasive because while the searches may overlap but they are not coextensive. The requirement is still deemed proper and is therefore made **FINAL.**

2. Claims 1-65 are pending. Claims 1-19, 25-32, 53, 54, 61 and 64 are under consideration. Claims 20-24, 33-52, 55-58, 60, 63 and 65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions.

Information Disclosure Statement

3. Applicants' Information Disclosure Statement, received 6/26/2003, paper # 5 is acknowledged. The references have been considered by the examiner. See attached 1449.

Drawings

4. This application, filed under former 37 CFR 1.60, lacks formal drawings. The informal drawings filed in this application are acceptable for examination purposes. When the application is allowed, applicant will be required to submit new formal drawings.

Specification

5. The use of the trademark "Vitaxin" has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 54 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein composition, does not reasonably provide enablement for a vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In the instant case claim 54 is drawn to a vaccine. The only given information in the specification in pages 42-43 is mentioning the general information on production of pharmaceutically acceptable carriers possible dosage information. No other information about protection from disease and how the vaccine was tested has not been provided by the applicants.

When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated base on that limitation. See in re Vaeck, 947 F. 2d 488, 495,20 USPQ 2d 1438, 1444 (Fed Cir, 1991).

Dorland's Medical Dictionary (29th Edition, 2000) defines "vaccine" as "a suspension of attenuated or killed microorganisms (bacteria, viruses, or rickettsiae), or of antigenic proteins derived from them, administered for the prevention, amelioration, or treatment of infectious diseases. In the instant case the applicants invention is not enabled for the prevention, amelioration, or treatment of infectious diseases. And one skilled in the art will not be able to make/and or use the invention without undue experimentation.

8. Claims 1-19, 25-32, 53, 54, 61 and 64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated protein construct as described on page 7, does not reasonably provide enablement for all possible active fragments thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches that the invention relates to a protein construct, especially an isolated or purified protein construct, comprising a pilus protein portion linked to an effector portion. However, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with the claims since the specification gives no guidance on or exemplification of how to anticipate the specific fragments. There is no further information in the specification in regard to the claimed active fragments. The claims of the instant application are not only drawn to

isolated protein construct but are also drawn to active fragments thereof. There is no guidance provided as to which how these active fragments selected. There is no guidance provided in the specification as how one would begin to choose "an active fragment".

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of prediction protein structure from a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is **not** routine in the art to screen for multiple substitutions or multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any protein and the result of such modifications is unpredictable based on the instant disclosure.

One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. Multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins.

The specification does not support the broad scope of the claims, which encompass all modifications and fragments because the specification does **not** disclose the following:

- an amino acid sequence for the claimed protein;
- the general tolerance to modification and extent of such tolerance;
- specific positions and regions of the sequence(s) which can be predictably modified and which regions are critical;
- what fragments, if any, can be made which retain the biological activity if the intact protein; and
- the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicant have **not** provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed protein in manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions or substitutions and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the proteins structure and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Amgen Inc v. Chugai Pharmaceutical Co Ltd. 927 F 2d 1200, 18 USPQ2d 1016

(Fed.Cir.1991) at 18 USPQ2d 1026-1027 and Exparte Forman, 230 U.S.P.Q. 546(Bd. Pat. App. & Int. 1986).

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-19, 25-32, 53, 54, 61 and 64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear what applicants intend in the recitation "including active fragments thereof". What constitute these active fragments? Are these active fragments of the protein construct or the pilus protein?

It is not clear what applicants intend in the recitation "said effector portion does not comprise all or part of either a bacterial pilus –protein or bacterial chaperone". What constitutes said effector portion?

Claims 2 and 10 recite the limitation "the usher-chaprone pathway" in the last line. There is insufficient antecedent basis for this limitation in the claims.

Claim 61 recites the limitation "The process of claim 59". There is insufficient antecedent basis for this limitation in the claims. Claim 59 is drawn to a protein construct not a process.

The use of the trademark "Vitaxin" has been noted in claim 64. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-5, 7-9, 25-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Jones et al. (Proc. Natl. Acad. Sci., Vol. 90, pp. 8397-8401, September 1993).

The claims are drawn to an isolated protein construct comprising a pilus protein wherein said pilus protein is a pilin selected from group consisting FimH and PapG.

Jones et al. teach an isolated protein construct comprising a pilus protein wherein said pilus protein is a pilin selected from group consisting FimH and PapG (see abstract, and pages 8398, 8399 and 8340). Jones et al. teach immunoglobulin and antibodies (see abstract and page 8400). The prior teach the claimed product.

Since the office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i. e., that the product of prior art does not possess the same material structure and functional characteristics of the claimed product). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

13. Claims 1-5, 7-9, 25-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Jones et al. (Proc. Natl. Acad. Sci., Vol. 92, pp. 2081-2085, March 1995).

The claims are drawn to an isolated protein construct comprising a pilus protein wherein said pilus protein is a pilin selected from group consisting FimH and PapG.

Jones et al. teach an isolated protein construct comprising a pilus protein wherein said pilus protein is a pilin selected from group consisting FimH and PapG (see abstract, and page 2084). Jones et al. teach immunoglobulin and antibodies (see abstract and page 2084).
The prior teach the claimed product.

Since the office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i. e., that the product of prior art does not possess the same material structure and functional characteristics of the claimed product). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

14. Claims 1-19, 25-32 and 53-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Thankavel et al. (Journal of Clinical Investigation, Vol. 100, No. 5, pp. 1123-1126, September 1997).

The claims are drawn to an isolated protein construct comprising a pilus protein wherein said pilus protein is a pilin selected from group consisting FimH and PapG.

Thankavel et al. teach an isolated protein construct comprising a pilus protein wherein said pilus protein is a pilin selected from group consisting FimH and PapG (see abstract, and page 1125). Thankavel et al. teach immunoglobulin and antibodies (see page 1125). Thankavel et al. teach a vaccine (see page 1125). The prior teach the claimed product.

Since the office does not have the facilities for examining and comparing applicants'

product with the product of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i. e., that the product of prior art does not possess the same material structure and functional characteristics of the claimed product). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Conclusion

15. No claims are allowed.

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Herren et al. Proc. Natl. Acad. Sci., Vol. 95, pp. 6037-6042, May 1998.

Langermann et al. Science., Vol. 276, pp. 607-611, April 1997.

Sauer et al. Science., Vol. 285, pp. 1058-1061, August 1999.

Kuehn et al. Science., Vol. 262, pp. 1234-1241, November 1993.

Saulino et al. Proc. Natl. Acad. Sci., Vol. 97, pp. 9240-9245, August 2000.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached from 7:30 AM - 4 PM on Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

January 11, 2004

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER